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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
CLFR:184USD1

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on June 13, 2007

Signature /Charles P. Landrum/

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Application Number	Filed
10/025,274	12/19/2001
First Named Inventor	
David N. Herndon	
Art Unit	**Examiner**
1633	Marvich, Maria

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 46,855
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

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June 13, 2007
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Arguments in Support of Pre-Appeal Brief Request for 10/025,274

I. The Obviousness Rejection of Instant Claim 43 is Inappropriate as a Matter of Law

In the final Action dated February 13, 2007, claim 43 (and dependent claims) were rejected on the basis of obviousness over Coffee (U.S. Patent 6,252,129) in view of McDonald *et al.* (U.S. Patent 6,120,799) or Yang *et al.* (Neuroreport, Vol 8, pages 2355-2358). Specifically, the Examiner alleges Coffee teaches application of a wound coverage material to injuries (including thermal injuries) and a matrix for the wound coverage material comprising growth factors and DNA. The Examiner further asserts that McDonald and Yang each teach the use of cationic liposomes containing cholesterol for the application of growth factors to external wounds. However, as the Examiner notes Coffee does not teach the use of cationic cholesterol containing liposomes (page 5, paragraph 2). Furthermore, neither McDonald nor Yang teach methods for treating an individual with a thermal (burn) injury or methods for treating a hypermetabolic response to a thermal injury. The Examiners assertion of obviousness is in appropriate for the following reasons.

First, as detailed in a previous response (November 22, 2006), there would be no motivation to combine Coffee with either McDonald or Yang to treat a hypermetabolic response to a burn injury. A skilled artisan seeking to modify the methods of Coffee to attenuate a hypermetabolic response would not be motivated to use liposomes of McDonald or Yang since these references do not concern thermal wounds nor do they concern methods for treating a hypermetabolic responses. Furthermore, neither Yang nor McDonald indicate that there is any

advantage in the use of a cationic cholesterol containing liposome. Thus, there is no explicit or implicit motivation to combine the references of record.

Second, there would be no reasonable expectation of success in the combination of any of the references of record in treating a hypermetabolic response resulting from thermal injury. Specifically, since there was no suggestion in the art regarding the ability of liposomes (to say nothing cationic cholesterol containing liposomes) to attenuate a hypermetabolic response, it would be completely unpredictable that the liposomes (with or without a nucleic acid encoding a growth factor) of McDonald or Yang could be used for such a purpose. There must be at least some degree of predictability for there to be a reasonable expectation of success (MPEP §2143.03, *In re Rinehart,* 531 F.2d 1048, 189 USPQ 143 (CCPA 1976)). In this case, as evidenced by the declaration of Dr. Jeschke, it was not predictable that cationic/cholesterol liposomes would be able to attenuate a hypermetabolic response. Thus, there would be no expectation of success in the combination of Coffee with of either McDonold or Yang. Hence, no *prima facie* case for obviousness has been set forth on the record.

Third, none of the references of record teach or suggest the surprising and unexpected results obtained with the methods of the instant invention. "A greater than expects result is an evidentiary factor pertinent to the legal conclusion of obviousness" *In re Corkill*, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985). Such a greater than expected result *is* realized using the methods of the invention. Specifically, the instant methods have a greater than expected effect on *burn wound healing* in that they attenuate the systemic hypermetabolic response. As described in the declaration of Dr. Jeschke (submitted with the November 22, 2006 response to Office Action) studies set forth in the instant application demonstrate an unexpected systemic effect achieved when cationic cholesterol containing liposomes (even with out nucleic acids

encoding growth factors) are administered locally at a wound site. These effects comprise short term weight gain, increases in serum protein and transferrin levels, and a decrease in serum levels of type I acute phase proteins and proinflammatory cytokines in treated animals all of which are favorable markers of recovery from injury. As described by Dr. Jeschke these effects constitute an attenuation of the systemic hypermetabolic response to injury. None, of the prior art of record teaches that locally administered cholesterol containing cationic liposomes could achieve these systemic results. Thus, the systemic effects of the instant methods on hypermetabolic response to injury constitutes a difference *in kind* that would not be predictable from the art of record. Hence, even with-out a nucleic acid encoding a growth factor compositions of the invention comprising cationic cholesterol containing lipids significantly reduced the hypermetabolic response. None of the art cited by the Examiner alone or in combination teaches any advantage to the use of cationic cholesterol containing liposomes much less the surprising and unexpected results achieved by the methods of the invention.

The Examiner has acknowledged the declaration of Dr. Jeschke that highlights the surprising results achieved with the use of cationic cholesterol containing liposome formulations but nonetheless finds Applicant's arguments "not persuasive." Specifically, the Examiner states that treatment of hypermetabolic effects is secondary to treatment of the burn injury. However, even if this is the case, the improved outcome resulting from the use of cationic cholesterol containing liposomes is no less surprising or unexpected. Furthermore, the Examiner states that the effects of cholesterol liposomes on hypermetabolic response are inherent in such liposomes and thus it is the burden of the applicant to show "a novel or non-obvious difference between the claimed products [method?] and the products [methods?] of the prior art," (page 8, of the February 13, 2007 Office Action). However, these arguments seem irrelevant since the supposed

prior art *methods* must necessarily be a result of the Examiner's combination of the Coffee and McDonald (or Yang) *methods*. As the Examiner acknowledges none of the cited references teach the use of cationic cholesterol containing liposomes (with or with a nucleic acid encoding a growth factor) for treating a burn injury or hypermetabolic response. Furthermore, there was no teaching or specific motivation in art to use such liposomes in a burn injury and certainly there would have been no expectation of the success much less any expectation of the surprising and unexpected results exemplified in the instant application. In view of the forgoing arguments and evidence Applicant's assert that the Examiner's rejection of the instant claims as obvious is erroneous. It is therefore requested that the pending claims be passed to allowance.